

REVIEWS

## Anaesthesia for carotid endarterectomy – general or loco-regional?

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### Abstract

Carotid endarterectomy has been widely used for the surgical treatment of carotid stenosis, and may be performed under either general or loco-regional anaesthesia. The greatest risks of carotid endarterectomy are the neurologic complications and the myocardial infarction.

Anaesthetic and surgical techniques are constantly under scrutiny to try to reduce the relatively high incidence of morbidity and mortality of an operation which in itself is only preventative. Loco-regional anaesthesia is an alternative to general anaesthesia which has attracted considerable attention amid claims of a reduction in operative morbidity and mortality. This review describes the problems and some solutions for providing loco-regional or general anaesthesia for carotid endarterectomy.

**Keywords:** carotid surgery, anaesthetic techniques, sedation, cerebral monitoring, complications

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### Introduction

Carotid endarterectomy (CEA) is among the most common vascular procedures. Recent studies have examined indications for CEA and the usefulness of multiple vascular procedures, and have compared general and loco-regional anaesthesia. Randomized prospective trials have confirmed that the efficacy of CEA exceeds 70% in patients experiencing a transient ischemic attack with an ipsilateral stenotic carotid lesion. When both carotid surgery and coronary revascularization are indicated, CEA can be performed two weeks before or concurrently with coronary artery

bypass. The greatest risk in CEA is of neurological complications (usually < 6%) and the risk of myocardial infarction (< 4%) [1].

Carotid stenosis is caused by atherosclerotic plaques that develop at the carotid bifurcation, resulting in the narrowing of the artery. Embolization of atheromatous material or thrombotic occlusion of the vessel can occur, resulting in transient ischaemic attacks, amaurosis fugax or cerebral infarction. The risk of such events is greatest in patients who are already symptomatic and in those with a greater degree of stenosis of the artery [2].

### Preoperative assessment

The medical management of patients with carotid stenosis includes control of coexistent hypertension and diabetes mellitus as well as advice on giving up smoking.

Preoperative hypertension is a risk factor for post-operative stroke and death, so patients with uncontrolled hypertension require close attention to perioperative arterial pressure control [3]. Specific figures for preoperative arterial pressure targets have not been defined from controlled trials, but a sensible target is

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that systolic and diastolic arterial pressures are  $\leq 180$  and  $\leq 100$  mm Hg, respectively [4].

The patient's neurological status should be assessed before operation, and neurological deficits documented, as differences detected in the postoperative period potentially require surgical re-exploration [5]. Anti-hypertensive medications should usually be continued except for angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists, but reductions in arterial pressure should be avoided in patients with neurological symptoms [4, 6]. Beta-blockers protect against perioperative cardiac complications in patients with a history of myocardial ischaemia, but this is offset by an increased risk of stroke in higher dose regimes and in patients who become acutely anaemic (although acute anaemia is rare in patients undergoing CEA) [7-9].

Antiplatelet therapy has a theoretical, therapeutic benefit both at the thrombogenic endarterectomy site and in the coronary circulation in high-risk vascular patients [1]. Patients should also be started on aspirin unless contraindications exist (150-300 mg/day for 2-4 weeks followed by 75 mg daily thereafter). There is certainly evidence in patients undergoing CEA of the benefits of dual antiplatelet therapy (aspirin combined with low-dose clopidogrel) to reduce the rate of micro-embolization after operation, and a Cochrane review of randomized trials found significant protection against stroke in patients receiving clopidogrel [10, 11]. However, due to the increased blood loss, surgery may take longer and careful consideration should be given to the risks and benefits of performing regional anaesthesia in these patients [12, 13]. There is no evidence available in the literature on the safety of performing CEA under general or regional anaesthesia techniques in patients receiving newer, faster onset and offset antiplatelet drugs such as ticagrelor or prasugrel or any other of the newer oral anticoagulants [14].

### Anaesthetic management

Carotid endarterectomy is now recognized as the treatment of choice in symptomatic patients who have a high degree of stenosis of the internal carotid artery ( $> 70\%$ ) [1]. It is also recommended in patients with less severe narrowing of the vessels in whom medical treatment has failed, or in those where irregular or ulcerated lesions are noted [2].

In asymptomatic patients who have a high degree of stenosis the indication for surgery is less clear. In these patients surgery offers improved outcome only in centres that have very low perioperative morbidity and mortality rates ( $< 3\%$ ), and in patients who represent a very low anaesthetic risk [15].

Besides the ablation of surgical pain, the main aim of the anaesthetic management should represent the protection of the brain and heart from ischemic events. The surgical intervention may be performed under either general or local-regional anaesthesia. Many reports have compared the impact of the two anaesthetic techniques on the patients' postoperative outcome without a certain conclusion being reached. Actually, each technique presents advantages and drawbacks.

### General anaesthesia

**Advantages.** Most anaesthetic agents reduce the cerebral metabolic rate, which may offer some degree of cerebral protection during the period of carotid cross-clamping. The benefits of this, however, may be restricted by the loss of cerebral autoregulation associated with volatile anaesthetic agents. Proponents of general anaesthesia cite neurological protection afforded by thiopental and volatile anaesthetic agents; the absolute perioperative control of ventilation (allowing control of arterial carbon dioxide concentration and its effects on the cerebral vasculature); and finally, the individual preferences of surgeons, anaesthetists, and patients [16, 17].

General anaesthesia is most comfortable for the patient and the surgeon. Many feel that general anaesthesia provides better operating conditions and improved surgical access, especially in patients with a high carotid bifurcation. It is also argued that it is less stressful than a regional procedure, which may benefit the patients with unstable angina and limited cardiovascular reserve [18].

**Disadvantages.** Cardiac complications are the primary cause of perioperative morbidity and mortality associated with CEA. Atherosclerosis is a systemic disease and patients with carotid stenosis have a high incidence of ischaemic heart disease. Anaesthetists usually aim to keep the mean arterial pressure 20% above the normal value for the patient to ensure adequate cerebral perfusion pressure during the period of carotid cross-clamping. General anaesthesia in these patients is associated with labile blood pressure, and the use of inotropes to maintain an elevated mean arterial pressure has been shown to increase the cardiovascular perioperative morbidity. This is presumably due to drug-induced increases in the myocardial workload [19].

Clinical assessment of neurological function is lost under general anaesthesia. Jugular venous oxygen saturation, transcranial Doppler-derived middle cerebral artery blood flow velocities, stump pressure measurements and continuous electroencephalogram monitoring are commonly used to assess cerebral blood

flow and function during cross-clamping. These techniques all require skilled interpretation, and when used in the awake patient both false-positive and false-negative results have been observed. Cerebral monitoring involves residual pressure after clamping, although that approach is unreliable. Other forms of haemodynamic (cerebral flow with  $^{133}\text{Xe}$ , transcranial Doppler, jugular  $\text{SvO}_2$ , conjunctival  $\text{PO}_2$ ) and electrical monitoring (EEG, somatosensory evoked potentials) are often unavailable, are expensive or require trained personnel [20].

Under general anaesthesia the use of shunts is based on stump pressure measurements and they are used more commonly than in the awaked patient. This is of concern because of the potential for thrombus formation, embolization of atheromatous material, intimal dissection, increased cross-clamping time and increased incidence of postoperative carotid artery stenosis that may result [18].

### Loco-regional anaesthesia

**Advantages.** The overwhelming advantage of performing CEA under loco-regional anaesthesia is that it allows awake cerebral function monitoring during the period of cross-clamping. Cerebral ischemia may manifest as loss of consciousness, seizures, confusion, dysarthria or a reduction in contralateral strength, and may be easily detected clinically. This is done by maintaining verbal contact with the patients and asking them to squeeze a squeaky toy held in the opposite hand and to move their toes. If the patient becomes symptomatic during initial trial period of cross-clamping, a shunt is inserted and decision made to proceed. In this situation elevation of the mean arterial pressure may also be beneficial [18].

Loco-regional anaesthesia (cervical plexus block or cervical epidural anaesthesia) can be monitored more reliably, allows therapeutic manoeuvres such as carotid unclamping, placement of an intracarotid stent, increasing of arterial pressure to be carried out. Regional anaesthesia decreases the incidence of intraluminal shunts. Blood pressure and heart rate are higher during cervical block than during general anaesthesia, but hypertension is more common during general anaesthesia. A randomized controlled trial comparing general anaesthesia and cervical block found no significant differences in mortality, myocardial infarction or transient ischaemic attacks. Regional anaesthesia is more cost-effective, given that less intensive care and shorter hospital stays are required [21].

When the procedure is performed under loco-regional anaesthesia, blood pressure is generally well maintained and is often noted to rise by 20 mmHg

during the period of cross-clamping. This suggests that some cerebral autoregulation is preserved, which may reduce ischaemic episodes [18].

Loco-regional anaesthesia offers both improved cardiovascular stability and the ability to monitor the patient for chest pain. Meta-analysis of non-randomized trials has shown that loco-regional anaesthesia is associated with lower cardiorespiratory complications in the perioperative period [22].

Loco-regional anaesthesia also offers potential financial advantages as intensive care is rarely required and the overall hospital stay is reduced. Loco-regional anaesthesia is well tolerated and this is supported by the results of a number of large clinical audits. In one series of 128 consecutive patients, over 90% said that they would have the same type of anaesthesia for future CEA [23].

**Disadvantages and complications.** The main disadvantages of loco-regional anaesthesia stem from complications of the technique itself. The procedure normally takes 1-2 hours and anxiety and physical discomfort caused by lying still for the length of time are potential problems.

Clearly not all patients are suitable for surgery under loco-regional anaesthesia, and in a minority general anaesthesia may be more appropriate. This may be due to psychological reasons, difficult neck anatomy (e.g. very obese) or simply because of patient refusal to undergo a procedure under loco-regional anaesthesia [18].

In performing loco-regional anaesthesia, local anaesthetic is injected close to a number of vascular and neural structures creating the potential for *various complications*. A thorough understanding of the anatomy involved is required for a reliable and safe technique.

**Intravascular/intra-arterial injection.** The vertebral artery and vein lie anterior to the cervical nerves at the point where the injection for the deep cervical plexus block are made. As little as 1-2 ml of local anaesthetic injected intra-arterially at this point may cause neurological symptoms, so the injection should be made very slowly, repeated negative aspirations should be performed and verbal contact maintained throughout to detect early signs of central nervous system toxicity [24].

**Local anaesthetic toxicity.** Local anaesthetic toxicity arising from absolute overdosage is unlikely when using the adequate volumes and concentrations of local anaesthetics. The addition of adrenaline further limits the systemic uptake of the local anaesthetic, but this remains a potential risk that must be considered, especially in frail elderly patients.

**Seizures.** Seizures occurring during CEA can be life-threatening, because of possible airway compromise and cerebral ischaemia due to increased cerebral

oxygen consumption. The cause of seizures during CEA is multifactorial and includes: local anaesthetic (LA) overdose, direct injection of LA into the artery (either by the surgeon or by the anaesthetist), or cerebral ischaemia. After operation, seizures may be a manifestation of the hyperperfusion syndrome, which generally requires aggressive anti-hypertensive treatment [25]. Seizures occurring intraoperatively due to intravascular injection of LA may be short in duration, with rapid subsequent recovery and do not necessarily preclude safely completing the operation [26].

*Subarachnoid/epidural injections.* It is essential that the needle is angled caudally when performing the deep cervical plexus block to avoid the danger of epidural or intrathecal injection. By doing it this way the needle will strike the tip of the transverse process below, rather than passing medially into the intervertebral foramen.

*Phrenic nerve block.* Hemidiaphragmatic paralysis has been shown to occur in more than 60% of patients undergoing CEA under cervical plexus block, although changes in arterial blood gases have not been shown to be clinically significant [24]. Patients may complain of a "heavy" sensation in their chest and reassurance and supplemental oxygen is all that is required.

*Recurrent laryngeal and vagus nerve block.* Studies have shown the incidence of recurrent laryngeal or vagus nerve block to be as high as 55% [24]. It presents as transient hoarseness and apart from the need to alert the surgeon to this before surgery, it is a harmless complication.

*Facial nerve block.* An ipsilateral facial nerve block may occasionally occur. This may cause confusion at the time of cross-clamping or in the recovery area, but it can be easily distinguished from a vascular complication as it occurs on the same side as the surgery.

*Cardiovascular instability.* Elevation of systolic blood pressure is often noted during arterial cross-clamping but this rarely requires treatment. Hypotension occurs much less frequently than in patients undergoing surgery under general anaesthesia and can usually be treated by fluids and vasoactive drugs, for this reason atropine and ephedrine should be readily available. Surgical stimulation or retraction of the vagus may cause bradycardia and even asystole in such circumstances. This is settled with the removal of the stimulus and intravenous atropine and ephedrine.

*Failure of block.* Performing regional blocks using ultrasound has been shown to be safer in terms of less LA toxicity and to have higher success rates than nerve-stimulator-guided blocks, but this has not yet been shown for cervical plexus blocks [27-29].

Deep/combined block has historically been more commonly associated with conversion to general

anaesthesia (GA) than superficial block [24]. If conversion to GA is required, this may usually be accomplished by the administration of suitable analgesics (e.g. remifentanyl) and propofol followed by airway control with a laryngeal mask airway and subsequent ventilation if required. This may arguably be safer and offer a better plan than a rapid sequence induction due to difficulties with intubation and potential haemodynamic consequences of intubation [30].

### **Sedation as supplement of local-regional anaesthesia**

Sedation is commonly administered to supplement the regional block during awake CEA, as inadequate analgesia or anxiety may increase the stress response and could precipitate adverse cardiovascular effects [31]. Judicious use of conscious sedation (communication maintained with the patient at all times) ensures patient comfort throughout the procedure while minimizing risks.

Several classes of sedative agents have been used including: opioids (remifentanyl, fentanyl), alfa-2 agonists (clonidine, dexmedetomidine), propofol, and, historically, butyrophenones (droperidol, haloperidol). The ideal sedative agent should reduce anxiety without causing respiratory depression, airway compromise, or haemodynamic instability, while the depth of sedation is altered rapidly [32].

Propofol target-controlled infusion produces effective, easily controlled sedation, easily titrated to an optimum level, while rapidly reducible to allow neurological monitoring during carotid cross-clamping [32].

Alfa-2 agonists are ideal drugs as in addition to sedation, they reduce analgesic requirements and are hypotensive agents with cardioprotective properties. Clonidine (1 mg/kg loading dose plus 1 mg/kg/h infusion) has been safely used in patients undergoing CEA without impairment of neurological monitoring, while decreasing the incidence of postoperative pain, hypertension, and neurological complications [33]. Dexmedetomidine is licensed in the USA as a sedative. It produces easily rousable sedation with no respiratory depression, reduces opioid administration, and has a short half-life allowing rapid titration to effect [34, 35]. Compared with other conventional sedatives, dexmedetomidine is associated with less intraoperative and immediate postoperative hypertension, fewer interventions for the treatment for hypertension, and less pain after operation. Suitable doses of dexmedetomidine for sedation during CEA are 0.2 mg/kg bolus followed by 0.2 mg/kg/h infusion [36, 37].

Carefully titrated sedation using small, repeated, intravenous doses of fentanyl (10-25 µg) and/or

midazolam (0.5–2 mg) should ensure a comfortable and cooperative patient during the operation [38].

Remifentanyl is the preferred sedative agent; it causes hypoventilation and therefore may cause hypercarbia, but this effect is minimized if the dose is titrated to effect [31]. Remifentanyl at doses up to 3 mg/kg/h produces a rapidly reversible and predictable sedation and analgesia while at the same time reducing local anaesthetics supplementation. Sedation must be minimal during cross-clamping to allow frequent neurological assessment. The practice is to turn off the remifentanyl sedation when the surgeon asks for heparin to be administered before cross-clamping, so that the patients are fully conscious when the period of carotid cross-clamping commences [39].

### Shunting during carotid endarterectomy

One of the goals for the anaesthetist during CEA is to protect the brain from ischaemic injury. The brain is particularly susceptible to ischaemic insult during carotid cross-clamping and therefore the anaesthetist and surgeon must be able to detect significant falls in cerebral perfusion and intervene appropriately. The commonest intervention in this situation is the insertion of a surgical shunt, which is not without associated risk. Several methods exist for monitoring cerebral perfusion during CEA although the ideal method has yet to be determined as none is perfect. Techniques available include continuous clinical assessment in the awaked patient, electroencephalography (EEG), somatosensory evoked potentials (SSEPs), transcranial Doppler (TCD), near infrared spectroscopy (NIRS), xenon blood flow and internal carotid artery stump pressure monitoring [40].

The period of carotid cross-clamping may be up to or even longer than 1 h, although there is considerable variation. Cerebral perfusion is most at risk during this period. Under general anaesthesia (GA), augmentation of arterial pressure to maintain cerebral perfusion is used by some, and augmentation of arterial pressure to 20% above baseline has been recently shown to reduce early postoperative cognitive dysfunction; however, this can precipitate myocardial ischaemia so must be done cautiously. Under GA, many surgeons choose to shunt all patients regardless of neurological state. In awaked patients, shunting is usually only performed if a neurological deficit develops after cross clamping. In such patients, two other treatment options are potentially available to avoid the need for carotid shunting [41, 42].

First, selective augmentation of the arterial pressure to normal, or up to 20% above normal, may reverse developing neurological ischaemia [43]. Secondly, the

administration of high concentrations of oxygen has been shown clinically to reverse the developing neurological deficit and to increase the ipsilateral cerebral oxygenation measured by cerebral oximetry during carotid cross-clamping [44, 45]. Using these additional management strategies, the percentage of patients requiring carotid shunting is reduced to 10% in patients undergoing awake CEA [15]. An awaked patient is the most reliable method for assessing neurology during carotid cross-clamping. Inadequate brain perfusion may present with loss or altered consciousness, confusion, agitation, dysphasia, seizures, and contralateral motor weakness [46].

An awaked patient can also notify the anaesthetist of cardiac symptoms such as a history of angina, or myocardial ischaemia can be detected on the ECG monitoring, thus allowing treatment and potential reversal of the condition [43].

Other neurological monitoring has been used in patients undergoing awake CEA. Bispectral index (BIS) monitoring has been used to predict the need for shunt placement and although the negative predictive value was 96.8%, the positive predictive value was only 56.3% [47]. Similarly, BIS monitoring during awake CEA has not been shown to be reliable in detecting cerebral ischaemia [48]. On the other hand, depth of anaesthesia monitors such as the Patient State Analyzer (PSA 4000, Physiometric Inc., North Billerica, MA, USA) which use multichannel analysis and can compare raw EEG from the left and right hemispheres have been successfully used to detect cerebral ischaemia during awake CEA [49].

Transcranial Doppler monitoring which is commonly used as a monitor of cerebral perfusion by monitoring middle cerebral artery blood flow during GA for CEA, has been used during awake carotid surgery to indicate developing cerebral ischaemia and to predict patients who may need shunting [50, 51]. In addition, TCD may be used to detect particulate and gaseous embolism intraoperatively and after operation and to monitor the development of postoperative hyperperfusion syndrome [20, 52, 53]. Patients at greatest risk include those with reduced preoperative cerebral blood flow due to bilateral high-grade carotid stenosis, unilateral high-grade carotid stenosis with poor collateral cross-flow, or unilateral carotid occlusion with contralateral high-grade stenosis. The hyperperfusion syndrome is thought to result from the restoration of perfusion to an area of the brain which has lost its ability to autoregulate [38].

The use of shunting during carotid endarterectomy is still controversial. While some surgeons advocate routine shunting, others prefer selective shunting or no shunting. Several large series have documented excellent results of CEA with routine shunting or without shunts. Others reported similar results with

selective shunting using transcranial Doppler (TCD), electroencephalogram (EEG) monitoring, carotid stump pressure (SP), cervical block anaesthesia (CBA), and somatosensory evoked potential (SSEP). The use of routine shunting and selective shunting was associated with a low stroke rate. Both methods are acceptable, and the individual surgeon should select the method with which they are more comfortable [40].

### Perioperative haemodynamic management

The cardiovascular manifestations associated with carotid surgery performed under GA and regional anaesthesia differ considerably [54]. Under GA, patients tend to be relatively hypotensive intraoperatively, commonly requiring vasopressor support [41]. After operation, GA patients tend to be hypertensive, due to emergence from anaesthesia and, perhaps, in pain. On the other hand, patients under regional anaesthesia are often relatively hypertensive intraoperatively, particularly during the cross-clamp period, but then relatively hypotensive after operation. These observations may be explained by cerebral autoregulation, which is probably still functioning in awaked patients [4].

Arterial pressure during carotid cross-clamping should not be allowed to decrease below the patient's 'baseline' and should be kept at or up to 20% above this. However, after carotid artery unclamping, hypertension should be avoided, to reduce the likelihood of hyperperfusion syndrome [24]. The choice of specific vasoactive drugs and reported thresholds for arterial pressure control depends on a variety of factors that include the patient's history, comorbidity, underlying heart rate, and drug history.

Metaraminol, ephedrine, and phenylephrine are commonly used to augment arterial pressure. A wide variety of drugs including hydralazine, glyceryl trinitrate (GTN), calcium channel antagonists, beta-blockers (labetalol, esmolol, atenolol), and alfa-2 agonists, such as clonidine, may be used to treat perioperative hypertension. Metoprolol should probably be avoided, due to pharmacogenetic variation in metabolism and the associated increased incidence of perioperative stroke [7, 55]. Calcium channel blockers and vasodilators may be beneficial in patients with ischaemic heart disease. GTN can increase cerebral perfusion pressure, despite a decrease in mean arterial pressure and nifedipine has caused precipitous decreases in arterial pressure and should be avoided in the acute management of hypertension in patients undergoing CEA [56].

Regional anaesthesia for carotid surgery has evolved over the last 15 years with new regional tech-

niques, novel methods of locating the cervical plexus, new drugs, and better management of the patient during the carotid cross-clamping. While regional anaesthesia has not been shown to be associated with better outcome than GA, there are differences in haemodynamic stability, the ease of neurological monitoring and the hospital stay.

### Conflict of interest

Nothing to declare

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## **Anestezia pentru endarterectomia carotidiană – generală sau loco-regională?**

### **Rezumat**

Endarterectomia carotidiană a fost extensiv utilizată pentru tratamentul chirurgical al stenozelor de carotidă și poate fi efectuată în anestezie generală sau loco-regională. Cel mai mare risc al endarterectomiei carotidiene sunt complicațiile neurologice și riscul de infarct miocardic acut.

Tehnicile anestezice și chirurgicale se află într-o permanentă și atentă monitorizare în încercarea de a reduce incidența ridicată a morbidității și mortalității cauzate de o intervenție chirurgicală aplicată cu scop exclusiv preventiv. Anestezia loco-regională ca o alternativă la anestezia generală a atras o atenție considerabilă, inclusiv pentru pretenția de a reduce morbiditatea și mortalitatea operatorie. Referatul de față descrie problemele și unele soluții pentru alegerea anesteziei loco-regionale sau generale pentru operația de endarterectomie carotidiană.

**Cuvinte cheie:** chirurgie carotidiană, tehnici anestezice, sedare, monitorizare cerebrală, complicații